



University of Groningen

Clinical and laboratory aspects of acute leukaemia

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Document Version

Publisher's PDF, also known as Version of record

Publication date:

1982

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Vries, E. G. E. D. (1982). Clinical and laboratory aspects of acute leukaemia. s.n.

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SUMMARY

This thesis deals with some clinical and laboratory aspects of acute leukaemia. The acute leukaemias are a group of haematologic neoplasms, characterized by the accumulation of blast cells. These cells are found not only in the blood, bone marrow and spleen, but may infiltrate any organ and tissue of the body. The accumulation of these cells leads to failure of the normal haematopoiesis.

In the *introduction* a review of the literature is presented concerning pathogenesis, diagnosis, etiology and treatment of acute leukaemia. Chapters II-IV deal with some clinical aspects of acute leukaemia in adults.

Chapter II reports the results in 34 patients with acute myeloid leukaemia treated with cytosine-arabioside, 6 thioguanine and daunorubicin. Nineteen patients were younger and 15 were older than 50 at the time of diagnosis. Complete remission was achieved in 20 of the 34 patients. Eleven patients were in the younger and 9 were in the older age group. With the treatment regimen used, remission rate and median survival and remission duration were the same in both groups. The rather short median interval (35 days) from institution of therapy to remission, and effective prophylactic antibiotic medication during the granulocytopenic period, may be the two principal reasons for these favourable results in older patients.

In *chapter III* the effect of combination chemotherapy for acute lymphocytic leukaemia in 25 adults is evaluated. All patients achieved complete remission. Twenty-two with vincristine-prednisone, while 13 patients also received daunorubicin. Three patients obtained remission only after treatment with cytosine-arabioside, 6 thioguanine and adriamycin. Despite central nervous system (C.N.S.) prophylaxis by intraventricular injections of methotrexate or cytosine-arabioside via an Ommaya reservoir, 2 out of 22 patients had a C.N.S. relapse. The median remission duration was 19 months, the median survival duration 38 months. Four patients could stop maintenance therapy, after 3 years, while still in remission.

In *chapter IV* the results are described of enteral nutrition by nasogastric tube in adult patients treated with intensive chemotherapy for acute leukaemia. In this study nutritional status 3 weeks after starting 20 induction courses of chemotherapy with enteral nasogastric tube feeding is compared to the nutritional status after 35 courses with a normal oral hospital diet. Tube feeding consisted of 2000-3000 Cal. daily of a hospital made pasteurized formula or a sterile factory product. In the group fed by nasogastric tube

the mean weight loss and decrease of serum albumin were significantly smaller and there were less patients with a severe weight loss of more than 5% during those 3 weeks. Bacterial contamination of the pasteurized hospital made formula occurred, leading to *Pseudomonas septicæmia* in one patient. It was concluded that during a short term catabolic state, sterile feeding by nasogastric tube can prevent weight loss and hypoalbuminaemia in most patients. Bacteriological control of the food and supply system is mandatory in granulocytopenic patients.

It is possible to study in vitro the granulocyte-monocyte and eosinophil precursor cells in bone marrow and peripheral blood. These cells form colonies in a two layer agar culture. In this way it is possible to study the normal haematopoiesis and the haematopoiesis during acute leukaemia.

In *chapter V and VI* the results with this method are reported focused on two aspects: the influence of lithiumcarbonate on granulocyte progenitor cells and the frequency of eosinophil colonies in healthy individuals and patients with acute leukaemia.

As lithiumcarbonate reduces the duration of neutropenia in patients receiving myelotoxic chemotherapy, we studied the in vitro influence of lithiumcarbonate on the granulocyte progenitor cell (Chapter V). A significant increase in the number and size of myeloid colonies was found in all patients, except in those with overt acute myelo-monocytic leukaemia. The effect of lithiumcarbonate was indirect in the sense that it increased the release of colony stimulating factor. However no effect on the number and size of the colonies and on the characteristic abnormal growth pattern was seen in acute myelo-monocytic leukaemia.

Apart from the well-known myeloid and eosinophil colonies after 10-14 days of culture we also observed eosinophil colonies after one day in cultures of peripheral blood and bone marrow (Chapter VI). This contributes a hitherto not described phenomenon. The critical condition to find these colonies was an adequate amount of nucleated cells per plate ($7 \cdot 10^5$ - $1 \cdot 10^6$). After 2-4 days these colonies degenerate. For the formation of these early eosinophil colonies (E.E.C.'s) colony stimulating factor is necessary. E.E.C.'s were found in healthy individuals and usually in an increased amount in patients with eosinophilia. Cultures of peripheral blood in patients with acute leukaemia showed in many patients no E.E.C.'s at all. The significance of this phenomenon remains to be investigated.